CLINICAL SYMPOSIUM

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Palliative Management of Mammary Carcinoma

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SURGICAL literature on mammary carcinoma is so largely concerned with the radical, curative approach to the disease that one is apt to forget that half or more of all women with this neoplasm are incurable when first examined. Further, there are certain forms of breast cancer which are technically operable but biologically incurable, and in which radical mastectomy may be harmful. The palliative management of this neoplasm is, therefore, as important statistically as the surgeon's attack on the potentially curable lesions.

The palliative results achievable in cancer of the breast are frequently impressive, for women can live with the disease effectively controlled for five to ten years or longer and continue to be socially and economically useful members of society. Not infrequently such prolongation of life is of immense importance to the family unit with young children. With an estimated 70,000 current cases of breast cancer in the United States, the clinical management of these patients is a recurring problem in general practice. The cooperation of physician, radiation therapist and, less often, the surgeon constitutes the desirable liaison in this problem.

CRITERIA OF INCURABILITY

Of first importance in establishing indications for palliative management are the criteria which determine incurability. Essentially, these criteria are those which make the patient ineligible for radical mastectomy, and are based either on the stage of the disease or its pattern of growth, as follows:

(A) A far advanced primary lesion in the breast.
(B) Extensive regional metastases.
(C) Distant metastases.
(D) Evidence of a highly malignant, rapidly growing, biologically incurable lesion.

Reducing these basic factors to specific situations, an arbitrary outline by which one may determine incurability can be offered.

DETERMINING FACTORS

(A) EXTENT OF PRIMARY LESION

1. *Extensive skin involvement.* Minimum skin attachment or retraction may be due to a scirrhus, superficially located tumor with dermal or subdermal sclerosis. Actual skin involvement means extensive permeation of local lymphatics and is as grave an omen as supraclavicular nodal metastases. "Peau d'orange" is a sign of late cancer. Satellite nodules in adjacent skin are a particularly bad sign.

2. *Fixation to pectoral fascia or chest wall.* Also a sign of late cancer, for if the disease has reached the pectoral fascia it is also in the subpectoral lymphatics and thus beyond the deepest plane of chest wall dissection in radical mastectomy.

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3. *Ulceration of skin.* Full thickness ulceration of any extent is usually a sign of inoperability, except in some slowly growing lesions without evidence of regional nodal metastases. In elderly women even with extensive ulceration the breast may be fully mobile and the regional nodes clear.

4. *Extension beyond the midline.* Occasional inner quadrant lesions near the medial periphery of the breast will have infiltrated across the midline, thus gaining access to the lymphatic system of the contralateral breast and axilla. This is an added hazard with inner quadrant lesions which frequently metastasize in the region of the internal mammary circulation.

(B) EXTENSIVE REGIONAL METASTASES

"Regional" lymph nodes include axillary and infra-clavicular groups. Supraclavicular nodes are distant, not regional.

1. *Bulky, fused axillary nodes.* Not an absolute contraindication to radical surgical treatment, especially if low in axilla or retropectoral. Fused nodes mean metastases no longer contained within intact lymph nodes, are practically synonymous with distant metastases and should have at least a trial with X-radiation.

2. *Extensive apical axillary nodal enlargement.* Sizable nodes at axillary apex are nearly certain indications of more distant spread.

(C) DISTANT METASTASES

1. *Supraclavicular lymphadenopathy.* Metastases to nodes above the clavicle are as certain a sign of incurability as is mediastinal node involvement. Enlarged supraclavicular nodes which are suspect, in otherwise operable cases, should be excised for histologic verification before radical operation on the breast.

2. *Pulmonary and Mediastinal.* Routine preoperative chest films should be obtained in all cases in which breast tumors which may be malignant are present.

3. *Skeletal. Order of Frequency:* (1) Ribs; (2) Spine (a) Lumbar, (b) Dorsal, (c) Cervical; (3) Pelvis; (4) Upper Femora; (5) Skull; (6) Humeri. Early metastases to bone are frequently not radiographically apparent. Preoperative skeletal surveys by X-ray are not mandatory except in the presence of persistent pain in possible metastatic sites.

4. *Hepatic.* May be apparent by examination. More frequent in inner quadrant lesions.

5. *Cerebral.* Headache or visual disturbance of progressive sort are usually present.

6. *Other sites.* Uncommon, usually not demonstrable.

(D) BIOLOGIC INCURABILITY

Certain forms of mammary carcinoma, approximately 8 to 10 per cent of all cases, are from the beginning rapidly growing and metastasizing and almost invariably lethal in two years or less. Two such lesions distinguished by certain clinical features, and which usually are not benefited by radical operation, may be recognized.

1. *Lesions developing during pregnancy or lactation.* The majority of these neoplasms are rapidly growing, with early regional and frequently distant metastases. Should be treated primarily by X-radiation.

2. *"Inflammatory" carcinoma.* So-called because of resemblance to acute inflammation of breast, with erythema of overlying skin. Such lesions may involve most of the breast in a few weeks. Primary lesion and local metastases are well controlled by x-radiation. Most of such patients die from distant metastases. Radical mastectomy seems to disseminate the disease more rapidly in some instances.

3. *Other anaplastic lesions.* Rapid growth of the primary lesion, or large axillary metastases even with a small breast lesion, may indicate a highly malignant, incurable neoplasm.

Other considerations related to the patient as a biologic unit may constitute inoperability. Severe cardiovascular disease is probably the most common. As in other concurrent disease, the risk must be measured in terms of expected longevity in relation to the anticipated progress of the breast cancer. Age in itself is not a contraindication to radical mastectomy, for many women in their eighth decade developing cancer of the breast have survived that long by reason of a constitutional integrity that enables them to withstand the operation.

ADAPTATION OF PALLIATIVE TREATMENT IN TERMS OF GROWTH PATTERN

From the foregoing outline it is apparent that mammary carcinoma is so variegated in its pattern of local growth and metastases that the palliative program must vary to a similar degree. In one patient the problem may be the reduction of growth of the tumor or the healing of ulceration in the breast, so that the impending terminal phase of the disease from distant metastases may be made less distressing. In another the problem may be that of an advanced local lesion of long duration, dilatory growth characteristics and without evidence of distant metastases, in which eradication or control of the local lesion may prolong life by years rather than months. In still others, the problem is that of palliative treatment of metastatic lesions, particularly in bone where adequate control of the disease may result in several more years of useful activity.

The measures available for the effective palliative treatment of breast cancer are still headed by x-radiation, both for the primary and secondary sites. Interstitial radium may be of value in occasional cases. Local surgical measures are of great value in selected patients, and combination of them with irradiation is often indicated. The use of sex hormones is still in an investigative phase, but present knowledge suggests that their status will be as complementary agents to irradiation. There are some distinct hazards in the large doses of androgenic and estrogenic hormone required for effective treatment, but the value of these agents in carefully selected patients, at certain age periods, seems amply demonstrated. The effectiveness of hormonal treatment is, however, highly variable, and the considerable number of therapeutic failures encountered should do much to discourage the premature popularity these agents now enjoy. Otherwise, palliative management requires in the later stages of the disease specific measures for a variety of complications, and an intelligent use of analgesic drugs on a progressive scale of effectiveness and dosage.

As encountered by the clinician, patients for palliative management may be bracketed as follows:

1. *Primary Cases*
   See groups A, B, C, D above
2. *Secondary (Post-Operative) Cases*
   Local Recurrence
   A. Chest Wall—10-25 per cent of post-operative cases
   B. Axillary—5-8 per cent of post-operative cases
   C. Distant Metastases—See Group C above

CLINICAL MANAGEMENT

DR. GUISS:

1. *A, B, D. Primary Local and Regional Disease*

The control of inoperable primary carcinoma of the breast with or without axillary metastases is basically a problem of management with x-ray therapy. X-ray ports are outlined over the primary lesion in such a way that the tumor can be crossfired through at least two ports, care being taken to irradiate as little lung tissue as possible. The axillary and supraclavicular metastases can also be crossfired in a similar way. It is often possible to bring the local and regional disease under clinical control for long periods of time. Five-year survivals without apparent disease have occasionally been obtained in this group of cases but are, of course, unusual. If the patient is young, as she often is, particularly in the biologically incurable group, x-ray castration should be part of the course of x-ray therapy. When there is extensive skin ulceration with associated infection and risk of hemorrhage, the patient not only presents a serious nursing problem but also technical difficulties in irradiation. Frequently it is preferable to do a simple mastectomy, thereby removing the foul, ulcerating mass before x-ray treatment is begun. It is usually possible to close the skin flaps but if necessary a split thickness graft may be utilized to close the defect. The care of the patient is thus much simplified and the palliative end result will be improved.

2. A. *Post-operative Skin and Chest Wall Recurrence*

It is generally agreed that if extensive post-operative skin or chest wall recurrence develops after a properly performed operation, the disease was not primarily operable, for of course it is not always possible to tell from a clinical standpoint whether a lesion is actually operable or not. If there are but one or two skin metastases, local excision of these lesions with a reasonable margin of normal tissue is probably justified. The treatment of choice, however, is x-radiation. One or two individual metastases in the skin can be treated by small ports using low voltage x-ray. However, since metastases are usually multiple, as a rule it is preferable to treat the entire operative area in which further skin nodules might be expected to develop. Radium needles can be inserted into areas in which there is recurrence in the skin, but there is always the danger of permanent injury to underlying bone and cartilage which sometimes

gives the patient more difficulty than the skin lesions themselves. Recently, some patients with recurrences in skin and soft tissue have been treated with high doses of estrogenic materials, and in some instances this has been followed by complete regression of the clinically apparent disease. Estrogenic therapy probably should be reserved for skin or soft tissue recurrence in elderly women many years post-menopausal who have already received X-radiation and whose skin cannot tolerate further therapy.

C. 3. *Skeletal Metastases*

The pain incident to skeletal metastases from breast carcinoma is somewhat variable, depending upon the extent and location of the lesions. There may be very extensive bone destruction without any symptoms at all. Occasionally, the first suggestion of bone metastases is a pathological fracture. More often the patient will complain of a dull ache of variable intensity, often worse at night and usually responding at first to mild analgesics. The symptoms of metastases to the spine are often mistaken for those of arthritis until X-ray films show the true nature of the process. Progressive collapse of the vertebral bodies causes pressure on the adjacent nerves, and symptoms of radiculitis then are added to the duller pain of the local disease. At times the patient may complain of severe pain in one of the bones and there may be nothing evident on radiographic examination. It is usually safe to assume in such cases that there is a metastasis present even in the absence of X-ray findings. Early bone metastases are not detectable by X-ray examination. By the time metastatic areas in the bone are discernible by X-ray examination, advanced destruction is present.

Despite the recent wave of enthusiasm for treatment of bone metastases by androgenic therapy, X-radiation still remains the treatment of choice for such lesions. Not only is the relief from pain prompt and lasting but also it is usually possible to arrest the progress of the metastatic lesion, often with complete recalcification. If the patients are pre-menopausal castration is usually indicated. Since X-ray castration seems to be as effective as surgical castration and is far more simply accomplished, it has largely replaced the surgical procedure. Androgenic therapy for skeletal metastases is currently popular. It may be used in any case regardless of the age of the patient. Dramatic response, often apparent within two or three weeks, is usually characterized by relief of pain, increased appetite, gain in weight and a sense of well-being. Unfortunately, the clinical progress of the patient may not parallel the symptomatic improvement and sometimes the metastatic lesions progress rapidly despite the symptomatic palliation. Calcium and Vitamin D have been administered in large quantities in an effort to facilitate the calcification of bony metastases but the end result of this additional therapy has not been convincing and the administration of these agents probably is not justified. In those cases in which there are metastases in the vertebral bodies, a properly fitted back brace will not only give the patient a great deal of relief from pain but will also protect the injured vertebral bodies from further strain thereby retarding progressive collapse of the bodies and permitting recalcification to take place following X-ray therapy or X-ray and androgenic therapy.

C. 2. *Pulmonary, Mediastinal and Pleural Metastases*

Occasionally, solitary and well localized metastatic deposits in the lungs may be treated by deep X-ray therapy. The results are unpredictable but at times the metastatic lesion may shrink to a fraction of its former size or entirely disappear. As a rule, pulmonary metastases are multiple and when the pleura becomes involved there is usually associated pleural effusion. If the amount of fluid is small, drainage is not necessary but if the vital capacity of the patient is interfered with by the volume of effusion, thoracentesis will afford a great deal of comfort. This procedure can be done either in the home or the office without the use of expensive or complicated apparatus.

There are isolated reports of regression of pulmonary metastases following both androgen and estrogen therapy, but use of these agents for the control of pulmonary metastases alone does not seem justified.

C. 4. *Liver and Other Abdominal Metastases*

The treatment of metastatic abdominal deposits from breast carcinoma is discouraging. When ascites develops the patient is not only subjected to abdominal discomfort but there is also elevation of the diaphragm with consequent impairment of vital capacity which may have been diminished already by pulmonary disease. Removal of the ascitic fluid as it collects will not only prevent abdominal discomfort but will relieve dyspnea in a patient with an already diminished vital capacity. Hormone therapy has not been used for the treatment of ascites. Recently we have seen a patient with extensive soft tissue recurrence associated with ascites. She was given high doses of estrogenic substance in the hope that this would control the skin recurrence. There was prompt regression of the skin metastases, and concommitantly the ascites was apparently competely absorbed, suggesting that there was regression of the intra-abdominal metastases also.

C. 5. *Cerebral Metastases*

Symptoms and signs incident to cerebral metastases depend entirely upon the location of the metastatic lesion. Careful neurologic examination may localize the metastatic deposit quite accurately. In cases where the progress of the disease appears slow and it is possible accurately to determine the site of the metastatic process, it is sometimes feasible to give deep X-ray therapy through small ports to the involved area. Results are extremely variable, but sometimes worthwhile palliation may be obtained.

SPECIAL CONSIDERATION OF MANAGEMENT

Hormone Therapy

The exact role of hormone therapy in the palliative treatment of mammary carcinoma is as yet unknown. It is at present on an experimental basis and care should be taken to be sure that the patient is benefited

rather than injured by such treatment. In light of the facts now known, it appears that patients with metastatic lesions in bone, without regard to age, are entitled to a trial of androgenic therapy. (Such treatment, however, has not replaced the known beneficial results that can be obtained by X-ray therapy to such lesions.) The dosage is usually 100 mg. of testosterone propionate given three times a week until a total of 3600 mg. has been administered, after which the patient is placed on a so called maintenance dose of 100 mg. weekly for an indefinite period. Symptomatic relief, usually apparent within two or three weeks, is characterized by relief of pain, gain in weight, increased appetite, diminished requirement for narcotics and a general sense of well-being. Objective signs of improvement do not necessarily parallel the relief of pain. Androgenic therapy must be controlled by roentgenographic and blood chemistry studies. In favorable cases there may be X-ray evidence of remineralization of the bone, but sometimes this does not occur even though there are subjective signs of benefit. Occasionally, the administration of high doses of androgen will increase the rate of bone destruction, and of course the medication should be stopped promptly in these cases. In the presence of a high value for serum calcium, treatment should be given cautiously. If the serum calcium drops to normal levels a good result can be expected; however, if it remains at a high level or a previously low serum calcium becomes elevated, androgenic therapy should be terminated at once.

Certain masculinizing effects are usually evident with such high dosage of testosterone. These include hirsutism, coarsening of the skin, voice change and often an increase in libido. These changes are most marked in younger women and may be so undesirable to the patient or to the family that continuance of testosterone therapy is not permitted. Occasionally, a patient, especially with high value for blood calcium, becomes intolerant to the drug, developing severe nausea, vomiting and other signs of intolerance, and of course androgenic therapy is not suitable for such patient.

Indications for the palliative use of estrogenic therapy are not yet definite. The information at present available suggests that estrogenic therapy should be reserved for patients in the older age group with soft tissue involvement. Beneficial effects have been largely restricted to regression in the size of inoperable primary lesions and in regression of soft tissue metastases. There appears to be also an improvement in the general physical condition of the patient. This favorable response, when it occurs, appears to be temporary and highly unpredictable. The preparation most commonly used is diethylstilbestrol given orally in doses of 15 mg. daily. Many patients do not tolerate the drug well. Estrogenic therapy should never be used for patients below the age of 60; in pre-menopausal women the administration of it may even accelerate the progress of mammary carcinoma. Frequently large doses of estrogens produce uterine bleeding, necessitating a diminution in the amount of the drug used.

Analgesics and Narcotics

Properly administered X-ray therapy is probably the most effective method of pain control in advanced cases of mammary carcinoma. When X-ray therapy is no longer effective and it is necessary to supplement its effects by medication, care should be taken in choosing a suitable drug. Many patients, particularly in the older age group, can be expected to live for months or years, and it is wise to reserve the stronger narcotics until they are absolutely necessary. As a rule, aspirin compounds supplemented with codeine are sufficient. Sometimes even aspirin alone will control the early pain. It is often possible to carry the patient on increasing doses of aspirin compounds with codeine up to the terminal stages of the disease. The large amount of codeine required not only diminishes the appetite but also constipates the patient, making special attention to bowel evacuation necessary. When codeine is no longer effective, a change can be made to either demerol, metapon or dilaudid, the choice depending upon the personal preference of the physician and the individual response of the patient to the drug. Some patients have less intolerance for one of the drugs than for another. Methadon, a new synthetic preparation, in doses varying from 2.5 to 10 mg. has been highly effective in the control of pain in the more advanced cases. The drug is less inclined to cause addiction than some of the others and does not interfere with the appetite, is less constipating and is quite inexpensive. Morphine with its euphoric and hypnotic effects should be reserved for the terminal stages of the disease.

Specific Measures for Pain Control

When there is severe pain originating in areas served by the lumbar and sacral levels of the spinal cord, intrathecal injections of alcohol will often give marked relief over a period of weeks or months. This procedure is of greatest value in cases where the pain is unilateral in distribution, although it may still be utilized when the pain is bilateral. The procedure is quite simple, but not without occasional undesirable sequelae such as disturbances in bladder and anal sphincter control, muscle paralysis and other undesirable complications. Severe localized pain such as that found in association with pathological fractures of the ribs can be effectively controlled by nerve block using one of the synthetic agents dissolved in oil for prolonged relief. Sometimes alcohol injections of individual nerves can be utilized to advantage. Cordotomy, an operative measure in which the spino-thalamic tract is severed, should be reserved for patients whose pain is severe and whose life expectancy exceeds at least six months. The operation, which is technically difficult and carries a certain amount of risk, should be done only on those patients in whom the measure of palliation would justify the procedure. Prefrontal lobotomy is a relatively new operation which has been recommended for intractable pain in certain selected cases. Application of the procedure has been quite limited, and it should be reserved for unusual cases.